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09/355,296	07/28/1999	Tanjore Balganesh	1103326-0576	6228

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WHITE & CASE LLP
PATENT DEPARTMENT
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EXAMINER	
HINES, JANA A	
ART UNIT	**PAPER NUMBER**
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/355,296	BALGANESH ET AL.	
	Examiner	Art Unit	
	Ja-Na Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 July 1999*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/27/99*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Status

1. Claims 1-6 are under consideration in this office action.

Claim Objections

2. Claims 2-6 are objected to because of the following informalities: Dependant claims 2-6 "a method", however the suggested claim language is to use of the article "The." Therefore the suggested claim language is "The method." Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claim 1 is drawn to a method of identifying a ligand of a bacterial, sigma^{70} subunit which comprises contacting the sigma^{70} subunit or a portion thereof comprising the anti-sigma binding region, with a test compound and a fusion protein of

an anti-sigma^{70} factor of bacteriophage T4, and determining whether the test compound binds competitively with the anti-sigma^{70} factor to the sigma^{70} subunit or portion thereof. The written description in this case only sets forth the portion of the sigma^{70} subunit obtained from *E. coli* or *S. typhimurium* as being the C-terminal 99 amino acids containing the anti-sigma binding region, therefore the written description is not commensurate in scope with the claims drawn to any portion thereof. Neither the specification nor the claims teach how to define the portions thereof. Neither the claims nor the specification teach how to obtain such portions. There is no guidance as to what portions can or cannot be used in the method being claimed. Thus, the resulting portion could result in a complexes not taught and enabled by the specification.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116). Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115). The specification teaches the structure of only a single representative species of such portions. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than having the anti-sigma binding region. Given this

lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

No information, beyond the characterization of the portion have been provided, which would indicate that applicants had possession of the claimed genus of any portion present in any said microorganism. The specification does not contain any disclosure of the structure of all the mutants or variants of any portions within the scope of the claimed genus. The genus of portions claimed is a large variable genus including mutants and variants, which can have wide variety of structures. The specification discloses the structure of only a single representative species of the claimed genus i.e., the C-terminal 99 amino acids containing the anti-sigma binding region from *E. coli* or *S. typhimurium*, which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

The MPEP does state that for generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP 2163. Although the MPEP does not define what constitute a sufficient number of representative, the Courts have indicated what do not constitute a

representative number species to adequately describe a broad generic. In Gostelli, the Court determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. In re Gostelli, 872 F.2d at 1012, 10 USPQ2d at 1618.

The written description in this case only sets forth the C-terminal 99 amino acids containing the anti-sigma binding region from *E. coli* or *S. typhimurium*, therefore the written description is not commensurate in scope with the claims drawn to portions thereof. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115). In view of these considerations, a person skilled in the art would not have viewed the teachings of the specification sufficient to show that applicants were in possession of the claimed portions. Therefore the full breadth of the claims fails to meet the written description provision of 35 USC 112, first paragraph.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) The preamble of the claims is drawn to a method for identifying ligands of a bacterial, sigma^{70} subunit which comprises contacting the sigma^{70} subunit or a portion thereof, where the recited steps within the method comprise: contacting the sigma^{70}

subunit or a portion thereof comprising the anti-sigma binding region, with a test compound and a fusion protein of an anti-sigma^{70} factor of bacteriophage T4; and determining whether the test compound binds competitively with the anti-sigma^{70} factor to the sigma^{70} subunit or portion thereof. Therefore, the goal of the preamble is not commensurate with the steps of the method that are drawn to identifying ligands. Therefore clarification is required to overcome the rejection.

b) The phrase "a fusion protein of anti-sigma^{70} factor of bacteriophage T4 is unclear. It is unclear if the fusion protein comprises the anti-sigma^{70} factor of bacteriophage T4 or if the fusion protein is a product of the anti-sigma^{70} factor of bacteriophage T4. Therefore clarification is required to overcome the rejection.

c) Claim 5 is drawn to the fusion protein also comprising glutathione-S-transferase. However it is unclear what is components of the fusion protein are. Therefore clarification is required to overcome the rejection.

5. Claims 1-6 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01.

a) The omitted steps in claim 1 are: There is no correlation step which correlates the identifying a ligand of a bacterial, sigma^{70} subunit and determining whether the test compound binds competitively with the anti-sigma^{70} factor to the sigma^{70} subunit or portion thereof. Therefore clarification is required to overcome the rejection.

b) The omitted steps in claim 2 are: There is no contact step. A contact step is required in order to provide for binding of the test compound, fusion protein and first and second antibodies. Therefore clarification is required to overcome the rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

6. Claims 1 and 3-6 are rejected under 35 U.S.C. 102(a) as being anticipated by Adelman et al, (1997. J. of Biol. Chem. Vol. 272(43): 27435-27443).

Claim 1 is drawn to a method of identifying a ligand of a bacterial, sigma^{70} subunit which comprises contacting the sigma^{70} subunit or a portion thereof comprising the anti-sigma binding region, with a test compound and a fusion protein of an anti-sigma^{70} factor of bacteriophage T4, and determining whether the test compound binds competitively with the anti-sigma^{70} factor to the sigma^{70} subunit or portion thereof. Claim 3 is drawn to the method of claim 1, wherein the sigma^{70} subunit or portion thereof is obtained from *Escherichia coli*. Claim 4 is drawn to the method wherein the anti-sigma^{70} factor has an amino acid sequence as shown in SEQ ID NO: 1. Claim 5 is drawn to the method wherein the fusion protein also comprises glutathione-S-transferase. Claim 6 is drawn to the method wherein the ligand is an inhibitor of a bacterial sigma^{70} subunit.

Adelman et al., teach the interaction of AsiA with both full-length sigma^{70}, and GSTσ(506) and measuring the fraction of AsiA bound to either sigma^{70} or GSTσ(506) (page 27,436, col. 2). Adelman et al., teach the test compound as being the AsiA protein. Adelman et al., teach contacting a glutathione-S-transferase (GST) GST-sigma^{70} fusion protein, containing GSTσ(506), the C-terminal 108 amino acids of sigma^{70}, fused to the GST moiety (page 27,436, col. 2). Adelman et al., teach a fusion protein of an anti-sigma^{70} factor of bacteriophage T4. Adelman et al., teach the determination of the competitive interaction between GSTσ(506), AsiA and sigma^{70} (page 27,436, col. 2). Adelman et al., teach the sigma^{70} is obtained from *E.coli* (abstract). Adelman et al., teach the anti-sigma^{70} factor having the full-length comprising the amino acid sequence as shown in SEQ ID NO: 1. Adelman teach the AsiA protein is known as an inhibitor of the sigma^{70} subunit (page 27,435, col.2).

Therefore, Adelman et al., teach the invention of claims 1 and 3-6.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1-4 and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Pahari et al., (July 7,1997. FEBS Letters Vol. 411:60-62).

Claim 1 is drawn to a method of identifying a ligand of a bacterial, sigma^{70} subunit which comprises contacting the sigma^{70} subunit or a portion thereof comprising the anti-sigma binding region, with a test compound and a fusion protein of an anti-sigma^{70} factor of bacteriophage T4, and determining whether the test compound binds competitively with the anti-sigma^{70} factor to the sigma^{70} subunit or portion thereof. Claim 2 is drawn to the method comprising: (i) immobilizing the sigma^{70} subunit or portion thereof on a matrix or solid support; (ii) adding the test compound and the fusion protein; (iii) adding a first antibody against the fusion protein; (iv) adding a labeled second antibody against the first antibody; and (v) determining the amount of second antibody bound to the (first antibody- fusion protein - sigma^{70} subunit or portion thereof) complex formed on the matrix or solid support. Claim 3 is drawn to the method of claim 1, wherein the sigma^{70} subunit or portion thereof is obtained from *Escherichia coli*. Claim 4 is drawn to the method wherein the anti-sigma^{70} factor has an amino acid sequence as shown in SEQ ID NO: 1 or SEQ ID NO: 2. Claim 6 is drawn to the method wherein the ligand is an inhibitor of a bacterial sigma^{70} subunit.

Pahari et al., teach contacting the sigma^{70} subunit with a test compound and a fusion protein of an anti-sigma^{70} factor of bacteriophage T4, and determining whether the test compound binds competitively with the anti-sigma^{70} factor to the sigma^{70} subunit (page 61). Pahari et al., teach contacting *AsiA* complex with anti-sigma^{70} and anti-AsiA antibodies as the first antibody (page 61, Fig. 3). The RNA polymerase contains sigma^{70} or a mutant anti-sigma^{70} (fusion protein) and is contacted with *AsiA*, the test compound (page 61, Fig. 3). Pahari et al., teach contacting to each, a polyclonal

antirabbit sigma^{70} antibody (the second antibody) for immunoprecipitation with Sepharose beads (the matrix or solid support) (page 61, Fig. 3). Pahari et al., teach the sigma^{70} subunit being obtained from *Escherichia coli* (page 60, col.1). Pahari et al., teach a small protein of bacteriophage T4, *AsiA* inhibits the sigma^{70} subunit which is known to be an anti-sigma factor (page 60, col.1).

Therefore, Pahari et al., teach the invention of claims 1-4 and 6.

Conclusion

8. No claims allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Jeffery Siew, can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ja-Na Hines
September 12, 2007

MARK NAVARRO
PRIMARY EXAMINER